standard;

P_s=Ceforanide activity in the ceforanide working standard solution in micrograms per milliliter;

C_u=Milligrams of sample per milliliter of sample solution; and

L=Percent lysine content of the sample. (Determined as described in § 436.349 of this chapter.)

(*b*) *Milligrams of ceforanide per vial.* Calculate the ceforanide content of the vial as follows:

$$\text{Milligrams of ceforanide per vial} = \frac{A_s \times P_s \times d}{A_s \times 1{,}000}$$

where:

A_u=Area of the ceforanide sample peak (at a retention time equal to that observed for the standard);

A_s=Area of the ceforanide peak in the chromatogram of the ceforanide working standard;

P_s=Ceforanide activity in the ceforanide working standard solution in micrograms per milliliter; and

d=Dilution factor of the sample.

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section, except reconstitute the vials with approximately 3.0 milliliters of diluting fluid A per each gram of antibiotic activity. Transfer approximately 1 milliliter from each of 20 vials into a sterile 500-milliliter Erlenmeyer flask containing 200 milliliters of diluting fluid A. Filter as described in paragraph (e)(1)(ii) of this section, except in lieu of filtering with three 100-milliliter quantities of diluting fluid A, rinse the filter membrane with three 100-milliliter portions of diluting fluid D followed by a final rinse with 100 milliliters of diluting fluid A.

(3) *Pyrogens.* Proceed as directed in § 436.32(b) of this chapter, using a solution containing 50 milligrams of ceforanide per milliliter.

(4) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(5) *pH.* Proceed as directed in § 436.202 of this chapter, using the solution obtained when the product is reconstituted as directed in the labeling.

[49 FR 25848, June 25, 1984; 49 FR 34347, Aug. 30, 1984; 49 FR 40006, Oct. 12, 1984, as amended at 55 FR 11583, Mar. 29, 1990]

§ 442.253 Cefotetan injectable dosage forms.

§ 442.253a Sterile cefotetan disodium.

The requirements for certification and the tests and methods of assay for sterile cefotetan disodium packaged for dispensing are described in § 442.53a.

[51 FR 20264, June 4, 1986. Redesignated at 59 FR 26941, May 25, 1994]

§ 442.253b Cefotetan sodium injection.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Cefotetan sodium injection is a frozen, aqueous, iso-osmotic solution of cefotetan and sodium bicarbonate. It contains one or more suitable and harmless buffer substances and a tonicity adjusting agent. Each milliliter contains cefotetan disodium equivalent to 20 milligrams or 40 milligrams of cefotetan per milliliter. Its cefotetan content is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of cefotetan that it is represented to contain. It is sterile. It contains not more than 0.17 endotoxin units per milligram of cefotetan. Its pH is not less than 4.0 and not more than 6.5. It passes the identity test. The cefotetan used conforms to the standards prescribed by § 442.52(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(A) The cefotetan used in making the batch for cefotetan potency, moisture, and identity.

(B) The batch for cefotetan potency, sterility, bacterial endotoxins, pH, and identity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

(A) The cefotetan used in making the batch: 10 packages, each containing approximately 500 milligrams.

(B) The batch:

(*1*) For all tests except sterility: A minimum of 12 immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*. Thaw the sample as directed in the labeling. The sample solution used for testing must be at room temperature.

(1) *Cefotetan potency*. Proceed as directed in §442.52(b)(1), except prepare the sample solution and calculate the cefotetan content as follows:

(i) *Preparation of sample solution*. Using a suitable hypodermic needle and syringe, remove an accurately measured portion from each container immediately after thawing and reaching room temperature and dilute with mobile phase to obtain a solution containing 200 micrograms of cefotetan per milliliter (estimated). Prepare the sample solution just prior to its introduction into the chromatograph.

(ii) *Calculation*. Calculate the milligrams of cefotetan per milliliter of sample as follows:

$$\text{Micrograms of cefotetan per milligram} = \frac{A_U \times P_s \times 100}{A_s \times C_U \times (100 - m)}$$

where:

A_U=Area of the cefotetan peak in the chromatogram of the sample (at a retention time equal to that observed for the standard);

A_S=Area of the cefotetan peak in the chromatogram of the cefotetan working standard;

P_S=Cefotetan activity in the cefotetan working standard solution in micrograms per milliliter;

C_U=Milligrams of sample per milliliter of sample solution; and

m = Percent moisture content of the sample.

(2) *Sterility*. Proceed as directed in §436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Bacterial endotoxins*. Proceed as directed in the U.S. Pharmacopeia bacterial endotoxins test.

(4) *pH*. Proceed as directed in §436.202 of this chapter, using the undiluted solution.

(5) *Identity*. The high-performance liquid chromatogram of the sample determined as directed in paragraph (b)(1) of this section compares qualitatively to that of the cefotetan working standard.

[59 FR 26941, May 25, 1994]

§442.255 Ceftriaxone injectable dosage forms.

§442.255a Sterile ceftriaxone sodium.

The requirements for certification and the tests and methods of assay for sterile ceftriaxone sodium packaged for dispensing as described in §442.55a.

[50 FR 10001, Mar. 13, 1985. Redesignated at 52 FR 44860, Nov. 23, 1987]

§442.255b Ceftriaxone sodium injection.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Ceftriaxone sodium injection is a frozen aqueous iso-osmotic solution of ceftriaxone sodium which may contain one or more suitable and harmless buffer substances. Each milliliter contains ceftriaxone sodium equivalent to 10, 20, or 40 milligrams of ceftriaxone per milliliter. Its ceftriaxone content is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of ceftriaxone that it is represented to contain. It is sterile. It is nonpyrogenic. Its pH is not less than 6.0 and not more than 8.0. It passes the identity test. The ceftriaxone sodium used conforms to the standards prescribed by §442.55(a)(1).

(2) *Labeling*. It shall be labeled in accordance with the requirements of §432.5 of this chapter.

(3) *Requests for certification; samples*. In addition to complying with the requirements of §431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(A) The ceftriaxone sodium used in making the batch for potency, moisture, pH, crystallinity, and identity.

(B) The batch for content, sterility, pyrogens, pH, and identity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

(A) The ceftriaxone sodium used in making the batch: 10 packages, each containing 500 milligrams.

(B) The batch:

(*1*) For all tests except sterility: A minimum of 10 immediate containers.